PCN18

INTERMITTENT VERSUS CONTINUOUS CHEMOTHERAPY FOR FIRST-LINE TREATMENT OF UNRESECTABLE METASTATIC COLORECTAL CANCER (CCRM): SYSTEMATIC REVIEW AND META-ANALYSIS

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OBJECTIVES: To perform a systematic review and meta-analysis of all randomized controlled trials comparing efficacy of Intermittent versus continuous chemotherapy (CT) for first-line treatment of unresectable Metastatic Colorectal Cancer (CCRm). **METHODS:** Several databases were searched, including MEDLINE, EMBASE, LILACS, and CENTRAL. The primary endpoint was overall survival (OS). The data extracted from the studies were combined by using Hazard Ratio (HR) with their corresponding 95% confidence intervals (CI95%). **RESULTS:** Overall, 733 references were identified and screened. The final analysis included 4 trials comprising 1,827 patients analyzed. There was no statistically significant difference between the groups (Intermittent vs continuous chemotherapy) on the analysis of overall survival (fixed effect: HR=1.03, CI95%=0.92 to 1.16; p=0.56). No heterogeneity was detected on this analysis (Chi2 = 2.88, df = 3 (P=0.41); I2 = 0%). **CONCLUSIONS:** Overall survival was similar between groups. The intermittent chemotherapy regimen provides better quality of life that the scheme is continued and probably cost saving.

PCN19

THE BROADER BURDEN OF HPV-RELATED DISEASE IN ENGLAND: A PRELIMINARY ANALYSIS

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OBJECTIVES: The Human Papillomavirus (HPV) is a known cause of cervical cancer and genital warts, and causes a proportion of vaginal, vulval, penile, anal, and head and neck (H+N) cancers. Quantifying the broader burden of HPV-related cancers is important as this group represents approximately 5.2% of all cancers. **METHODS:** Using cancer registry data covering the population of England (2003-2008), we examined incidence of HPV-related cancers. HPV-associated sites were identified (cervix, vulva, vagina, anus, penis and H+N) and grouped according to ICD-O-3 site. Incidence rates were age-adjusted (ASR) to the European standard population by the direct method and 95% Confidence intervals (95% CI) calculated using STATA SE11.0. A literature review was conducted to ascertain the percentage attributable to HPV for each cancer type. Over 300 articles were reviewed and graded by relevance, sample size, and date. **RESULTS:** ASRs for HPV-related cancers were: vagina/vulval cancers: 0.33(95% CI 0.3-0.4) and 1.4(95% CI: 1.3-1.4) per 100,000 females. Penile cancer: 0.8(95% CI: 0.7-0.8) per 100,000 males. Anal cancers: 10.8(95% CI:10.7-11.1) males and 6.0(95% CI:5.8-6.0) females per 100,000. Base of tongue and lingual tonsil: 0.06(95% CI:0.06-0.07) males and 0.02(95% CI:0.01-0.02) females per 100,000; tonsil: 0.11(95% CI:0.10-0.12) males and 0.03(95% CI:0.03-0.04) females per 100,000; oropharynx: 0.05(95% CI:0.05-0.06) males and 0.02(95% CI:0.01-0.02) females per 100,000. Estimates reported in literature for percentage of HPV-attributable cases ranged from 70-100% for cervical, 27-76% vulval, 70-90% vaginal, 40-54% penile, 76-90% anal, and 11-72% for HPV-associated H+N cancers. The most commonly reported strains were HPV 16, 18, 31, and 33. **CONCLUSIONS:** The incidence of HPV-related cancers represents a significant burden. Recent incidence estimates are similar to 2002 estimates, apart from an increase in anal cancers. Estimates of the HPV-attributable percentage for each cancer and projected prevalence will be used to assess the impact of implementing a quadrivalent HPV vaccination programme in England.

PCN20

SYSTEMATIC REVIEW OF SKELETAL RELATED EVENTS IN BREAST CANCER

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OBJECTIVES: Metastatic bone lesions lead to an increase in the risk for skeletal related events (SREs), including pathologic fracture, spinal cord compression, hypercalcemia of malignancy, and severe bone pain requiring palliative radiotherapy or surgery to bone. Twenty-nine percent of breast cancer patients with bone metastases develop SREs. Our objective was to systematically review the literature on the impact of SREs on pain, quality of life (QOL), morbidity, survival and cost in breast cancer patients. **METHODS:** We searched PubMed, limiting to peer-reviewed English-language human studies published in 2000-2010. The search was based on a SRE definition accepted by the U.S. Food and Drug Administration and European Medicines Agency. Articles were included if they were randomized-controlled trials, clinical trials with appropriate control group, systematic reviews, meta-analyses, case-series or economic analyses, and were excluded if they did not provide interpretable results on outcomes of interest. **RESULTS:** A total of 209 articles were screened, of which 131 were excluded, and 78 were abstracted. No studies, outside of bisphosphonate trials, were identified that examined the impact of SREs as a group on clinical outcomes. Bisphosphonate treatment reduced SREs, and hence improved pain and QOL. Literature indicated that presence of pathologic bone fractures is correlated with increased risk of death. Spinal cord compression significantly impaired ambulatory function and shortened survival of these patients compared to historical controls. Radiation therapy improved pain and QOL while bone surgery was shown to improve pain and function with vertebrectomy. Limited evidence suggested treatment cost of SREs is $14,000 (95% CI: $11,000-$17,000) per patient. **CONCLUSIONS:** Presence of clinical SREs is associated with worse morbidity and survival, while their treatment is associated with improved pain, QOL and morbidity among breast cancer patients. SREs appear to increase cost of treatment substantially.

PCN21

SYSTEMATIC REVIEW OF SKELETAL RELATED EVENTS IN PROSTATE CANCER

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OBJECTIVES: Between 65-75% of patients with prostate cancer experience metastatic bone disease. Metastatic bone lesions increase risk for skeletal related events (SREs), which include clinical SREs (pathologic fracture, spinal cord compression, hypercalcemia of malignancy) and treatments of clinical SREs (radiotherapy or surgery to bone) resulting from severe bone pain. Our objective was to systematically review the literature on the impact of SREs on pain, quality of life (QOL), morbidity, survival and cost in prostate cancer patients. **METHODS:** We searched PubMed, limiting to peer-reviewed English-language human studies published in 2000-2010. The search was based on SRE definition accepted by the US Food and Drug Administration and European Medicines Agency. Articles were included if they were randomized-controlled trials, clinical trials with appropriate control group, systematic reviews, meta-analyses, case-series or economic analyses, and were excluded if they did not provide interpretable results on outcomes of interest. **RESULTS:** A total of 209 articles were screened, of which 131 were excluded, and 78 were abstracted. No studies, outside of bisphosphonate trials, were identified that examined the impact of SREs as a group on clinical outcomes. In bisphosphonate trials, patients with SREs had significantly more pain and worse 1-year survival compared with no SREs. Pathologic bone fractures significantly decreased QOL and were associated with increased risk of death. Although spinal cord compression (SCC) has a significant impact on pain, improvement in morbidity may be achieved if SCC is treated. SCC is associated with significant decreases in patient survival. Radiation therapy improved pain and possibly QOL while bone surgery improved pain. Limited evidence suggested SREs increased cost by approximately €7,000 (Euros) and $12,000 (USD). **CONCLUSIONS:** Clinical SREs are associated with worse clinical outcomes, including pain, QOL, morbidity and survival, while treatment of clinical SREs is associated with improved pain and QOL among prostate cancer patients. SREs appear to increase cost substantially.

PCN22

SAFETY PROFILE OF BEVACIZUMAB IN METASTATIC COLORECTAL CANCER

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OBJECTIVES: To assess the overall risk of bevacizumab related adverse events in patients with metastatic colorectal cancer (mCRC). **METHODS:** A systematic review of the literature was conducted. The selection criteria of the studies for this review were: health technology agencies reports, meta-analysis, systematic reviews, randomized controlled trials (RCTs) and observational studies in patients treated with bevacizumab for mCRC. MEDLINE, EMBASE, the Cochrane Library, and CRD databases were searched until June 8, 2011. The selection of the studies, quality assessment, data extraction and data analysis were done independently by two authors. Disagreements were resolved by a third reviewer until consensus was obtained. **RESULTS:** To evaluate the safety profile of bevacizumab, two systematic reviews with meta-analysis and two observational studies were included (the BEAT and the BRiTE studies). A total of 3271 patients were included in one meta-analysis, which evaluated the risk of fatal adverse events (FAE) and 3,385 patients were included in the other meta-analysis, which evaluated any grade of toxicity. An increased risk of FAE was not observed between patients with mCRC receiving bevacizumab in combination with chemotherapy and patients receiving chemotherapy alone [Relative Risk (RR):1.21 Confidence Interval (CI) 95%: 0.65-2.24]. Patients treated with bevacizumab had an increased risk of developing grade 3-4 hypertension (RR: 4.27; CI95%: 2.80–6.51), any grade gastrointestinal perforation (RR: 5.04; CI95%: 1.72–14.79), grade 3-4 arterial thromboembolic events (RR: 1.23; CI95%: 0.93–1.62), and discontinuation because of grade 3-4 adverse events (RR: 1.21; CI95%: 1.03–1.43). The results from the observational studies were consistent with the data reported in the meta-analysis. **CONCLUSIONS:** Although the risk of FAE was not increased with bevacizumab in patients with mCRC, grade 3-4 hypertension, any grade gastrointestinal perforation, grade 3-4 arterial thromboembolic events, and discontinuation due to grade 3-4 adverse events were higher in the bevacizumab group.

PCN23

SURVIVAL ANALYSES ADJUSTED FOR CROSSOVER IN RELAPSED MULTIPLE MYELOMA: RESULTS OF THE APEX TRIAL

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OBJECTIVES: An interim analysis of APEX, a phase III randomized, open-label clinical trial, demonstrated superiority of bortezomib over high-dose dexamethasone in terms of time to disease progression (TTP). According to the original study protocol, patients were allowed to cross over on disease progression. Following interim analysis, patients could cross over regardless of the disease status. The ITT analysis of overall survival (OS) may therefore result in a biased estimate of the treatment effect. This study aimed to adjust the analysis for crossover. **METHODS:** The Iterative Parameter Estimation (IPE) algorithm using a Weibull distribution was selected as the primary analysis based on the findings from a simulation study (Morden et al). The IPE algorithm using a Gompertz distribution and the Rank

Preserving Survival Time (RPSFT) model were used as secondary analyses. The Inverse Probability of Censoring Weights (IPCW) method and the Cox model using treatment as a time-dependent covariate were used as sensitivity analyses. **RESULTS:** Overall, 71% of patients randomized to dexamethasone crossed over to bortezomib. The primary analysis led to a hazard ratio of 0.59 (95%CI: [0.32,0.86]) for bortezomib versus dexamethasone, compared to 0.77 (95%CI: [0.61,0.97]) using the ITT approach. The results of the secondary analyses were consistent with the primary analysis. The IPCW provided results, which were very sensitive to the choice of the time interval. Lastly, the Cox model with treatment as a time-dependent variable resulted in a counter-intuitive higher hazard ratio than the ITT analysis, consistent with results from simulation studies indicating this approach is biased. **CONCLUSIONS:** Adjusting for crossover led to a decrease of the hazard ratio from 0.77 to 0.59, and resulted in wider confidence intervals than the ITT analysis. Additional analyses are required to assess the performance of the IPCW method compared to the IPE algorithm and the RPSFT model under different scenarios.

Cancer – Cost Studies

PCN24

BUDGET IMPACT MODEL FOR RARE CANCER TREATMENT: CASE IN POINT CUTANEOUS T-CELL LYMPHOMA

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OBJECTIVES: Develop budget impact model to forecast total cost of treatment for cutaneous T-cell lymphoma (CTCL) for US public and private payer. **METHODS:** The clinical efficacy and safety data were obtained from the published pivotal study results. Costs of adverse events were estimated based on claims database analysis, AHRQ's HCUP and CMS Medicare 2009 databases. Drug cost was estimated based on 2011 AWP price. Epidemiology data were obtained from NCI-SEER and CDC databases. A budget impact model was implemented over a period of five years, based on a stable population and on different penetration and substitution rates of newly approved therapy. Model was developed in excel based format. Blinded Model design and outputs were tested with payers and KOLs. **RESULTS:** For rare cancers such as CTCL, the budget impact of treatment with targeted cancer therapies is in the range of $460,000-$530,000 per 1 million covered lives. The per patient per member (PPPM) budget impact of this treatment is 46-53 cents. Medical cost offsets were estimated but were insignificant compared to total cost of treatment. US payers rated PPPM output as the one of the most important relevant outputs of model. **CONCLUSIONS:** This budget impact model shows that new treatments for rare forms of cancer are likely to have minimal budget impact on payers. PPPM based outputs are more relevant to payers, than per patient treatment costs. However, an emerging concern is the total budget impact of all therapies indicated for ultra-orphan disorders, which might be an important consideration for future models.

PCN25

BUDGET IMPACT ANALYSIS OF SWITCHING TO DIGITAL MAMMOGRAPHY IN A BREAST CANCER POPULATION-BASED SCREENING PROGRAM

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OBJECTIVES: Digital mammography is costlier than screen film mammography but presents benefits at the technological and logistic level. The aim of this study was to analyze the budget impact and the health benefits of the introduction of digital mammography in a population-based breast cancer screening program. **METHODS:** A discrete-event simulation model was implemented including the processes under a breast cancer screening program and the natural history of breast cancer. The screening events included: invitation (biennial) of the target population (women aged 50-69 years), participation, screening test, confirmatory tests after a positive mammography result, cancer diagnosis and treatment. Natural history of breast cancer included the following health states: no cancer, preclinical (non symptomatic) cancer, clinical (or symptomatic) cancer and death. Digital and analogical mammography had the same sensitivity, but different specificities were applied according to type of mammography and also initial or successive screening. Results were collected during a 20-year screening scenario. **RESULTS:** A total of 90,575 women were screened under both techniques during the simulated 20 years. This population resulted in more than 262,500 screening mammograms. The recall rate was 5.9% under digital mammography and 6.4% under analogical mammography, while the numbers of confirmatory tests needed were 23,728 and 32,697, respectively. The cancer detection rate was 0.7% for both techniques. Digital mammography saved 1.909.167 euros in additional tests, while it was 1.026.807 euros more expensive in screening mammograms and presented similar costs of treatments. **CONCLUSIONS:** Results suggest that, although population-based breast cancer screening with digital mammography is costlier in terms of screening mammographies, it saves money in terms of additional tests needed. The health benefits are similar to those of conventional analogical mammography, but it reduces the number of additional tests needed, which represent a clear benefit to participating women.

PCN26

LONG-TERM FISCAL IMPLICATIONS OF MEPACT IN THE TREATMENT OF HIGH-GRADE NON-METASTATIC OSTEOSARCOMA: A BUDGET IMPACT MODEL AND A LIFETIME TAX PERSPECTIVE

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OBJECTIVES: The addition of MEPACT as an add-on treatment to adjuvant chemotherapy in the treatment of high-grade non-metastatic osteosarcoma after macroscopically complete surgical resection has been shown to significantly increase overall survival of young patients. This study assessed the costs (drug and administration) and the long-term financial impact on the UK (UK) government of introducing MEPACT. **METHODS:** Based on the cost of MEPACT and using survival rates derived from a clinical trial, we projected the net budgetary impact of MEPACT compared to no MEPACT. Further, we modelled the net tax contribution to the state of a surviving patient over a lifetime by subtracting direct government transfers that are made to the individual (child benefit, education etc) from the individual's gross tax contribution based on average anticipated earnings. **RESULTS:** Using UK incidence rates of osteosarcoma the model estimated approximately 54 newly diagnosed non-metastatic cases per year. Assuming that 38 doses of MEPACT (calculated from trial data) are added to the treatment regimen of 50% of patients at a cost of £91,189 , the expected 1-year cost would be UK £3,972k compared with £1,450k had all patients been treated without MEPACT. Administration costs accounted for 3% of total costs. The lifetime discounted value of net taxes from a 14 year old patient treated with MEPACT is £79,000. The breakeven age, defined as the point at which the net tax contribution becomes greater than zero, is approximately 41 years. **CONCLUSIONS:** The additional budget impact due to MEPACT is mainly due to the cost of the drug. From the tax calculations, we conclude that investment in MEPACT does not negatively impact the long run fiscal budget of the UK government. Conversely, by taking a broader government perspective over an average lifetime, a surviving patient returns a positive net value to the State.

PCN27

BUDGET IMPACT ANALYSIS FOR CHRONIC MIELOID LEUKEMIA THERAPY IN BULGARIA

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OBJECTIVES: To evaluate the budget impact of nilotinib for newly diagnosed patients with chronic myeloid leukemia (CML) for the health care system in Bulgaria. **METHODS:** Current standard of therapy (imatinib) is compared with the newly authorized for sale nilotinib and dasatinib used as a first line therapy. Cost of yearly pharmacotherapy and adverse drug reactions management have been calculated for 3 years for different proportions of newly diagnosed patients with CML in chronic phase. The exchange rate is 1 BGN = 0.51 EUR. **RESULTS:** Clinical studies shows significant benefits from nilotinib but the question remains if it is worth the cost of therapy. Calculation of the yearly pharmacotherapy cost per 100 patients arranges the medicines in monetary value order as follows: 5,398,092 BGN for imatinib, 6,564,681 BGN for nilotinib, and 8,365,872 BGN for dasatinib. Weighed cost by the probability of appearing of the ADR is 733.26 BGN for imatinib, 509.75 for nilotininb, and 1,010.29 BGN for dasatinib. The relative share of patients treated with nilotinib in first line is 12% for the first year, 32% for the second, and 38% for the third year. The introduction of nilotinib will change the budget for all patients with CML to 6,895,316 in comparison with 6,725,246 BGN before the introduction, to 7,177,671 BGN in the second year, and to 7,262,378 BGN in the third year. Thus the over all increase for the observed 3 years will be within 179,044 BGN. **CONCLUSIONS:** The introduction of nilotinib as first line therapy for patients with newly diagnosed CML will lead to relatively small increase in the health care budget in Bulgaria compared to the clinical benefit in terms of achievement of deeper response, improvement of overall survival and less disease progression.

PCN28

CAPECITABINE FOR THE TREATMENT OF BREAST CANCER IN PRIVATE HEALTH SYSTEM IN BRAZIL: COST ANALYSIS BASED ON REAL WORLD DATA

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OBJECTIVES: Capecitabine (C) is approved in Brazil for the treatment of breast cancer (BC), 2nd or subsequent lines. In the private sector, it's not often used, due to the fact that health insurance plans (HI) do not offer coverage for oral (PO) chemotherapy (CHEMO), only for intravenous (IV). Our aim was to determine if the use of C could spare costs if adopted by HI. **METHODS:** We searched Evidencias Database for BC patients eligible for the use of C, in the year of 2008. This database has information from over 2 million of users of 14 HI. We identified the IV CHEMO actually used and the costs paid. Then, based on the data of each individual patient and in the length of use of CHEMO, we calculated the associated costs in a scenario where C replaced the IV CHEMO used. Also, we performed some sensitivity analysis based on different percentages of substitutions of IV by PO chemo. We considered only the prices of drugs. **RESULTS:** We found 518 BC patients eligible for C use. These patients received 3581 cycles of chemotherapy (Paclitaxel, Docetaxel, Gemcitabine, Vinorelbine, Doxorubicin). The total cost for these treatments were US$ 5 364 000. If C replaced 100% of the IV CHEMO, the total cost would drop to US$2,078,000, 62% smaller than the IV alternative. In a simulation, where 60% of the patients would use the IV option and 40% would use C, the total cost would also be smaller: US$4,050,000, 25% smaller than when IV route is used exclusively. **CONCLUSIONS:** The adoption of C by HI in Brazil is cost-saving for BC patients.

PCN29

BUDGETARY IMPACT OF ADOPTION OF ERLOTINIB FOR LUNG CANCER IN THE PRIVATE HEALTH INSURANCE MARKET IN BRAZIL: A REAL WORLD DATA ANALYSIS